

10/031,037

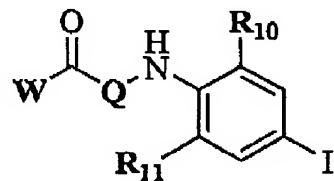
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CURRENTLY PENDING CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application. This listing does not amend the claims.

Listing of claims:**1 and 2 (canceled).**

3 (previously presented). A method for treating chronic pain, wherein said chronic pain is a type of neuropathic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of the following formula (I):



(I)

wherein

W is OR₁, NR₂OR₁, NR_AR_B, NR₂NR_AR_B, O(CH₂)₂₋₄NR_AR_B, or NR₂(CH₂)₂₋₄NR_AR_B;

R₁ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)-C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)-C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or (CH₂)₂₋₄NR_CR_D;

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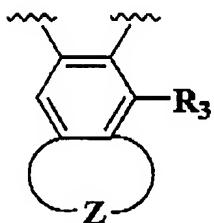
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R₂ is H, C ₁₋₄ alkyl, phenyl, C ₃₋₆ cycloalkyl, C ₃₋₆ heterocyclic radical, or (C ₃₋₆ cycloalkyl) methyl;

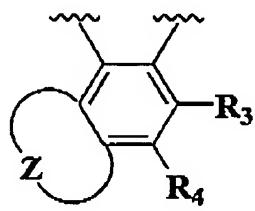
R_A is H, C ₁₋₆ alkyl, C ₃₋₈ alkenyl, C ₃₋₈ alkynyl, C ₃₋₈ cycloalkyl, phenyl, (C ₃₋₈ cycloalkyl)C ₁₋₄ alkyl, (C ₃₋₈ cycloalkyl)C ₃₋₄ alkenyl, (C ₃₋₈ cycloalkyl)C ₃₋₄ alkynyl, C ₃₋₈ heterocyclic radical, (C ₃₋₈ heterocyclic radical)C ₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C ₁₋₄ alkyl, (aminosulfonyl)C ₁₋₆ alkyl, (aminosulfonyl)C ₃₋₆ cycloalkyl, [(aminosulfonyl)C ₃₋₆ cycloalkyl]C ₁₋₄ alkyl, or (CH₂)₂₋₄ NR_CR_D;

R_B is H, C ₁₋₈ alkyl, C ₃₋₈ alkenyl, C ₃₋₈ alkynyl, C ₃₋₈ cycloalkyl, or phenyl;

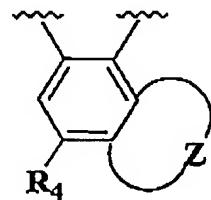
Q is one of the following formulae (i) – (iii):



(i)



(ii)



(iii)

R₃ is H or F;

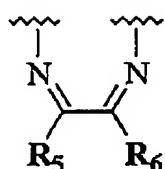
R₄ is halo, NO₂, SO₂NR_O(CH₂)₂₋₄NR_ER_F, SO₂NR_ER_F, or (CO)T;

T is C ₁₋₈ alkyl, C ₃₋₈ cycloalkyl, (NR_ER_F)C ₁₋₄ alkyl, OR_F, -NR_O(CH₂)₂₋₄NR_ER_F, or NR_ER_F;

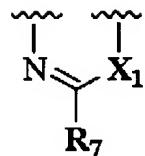
Z is one of the following formulae (iv) – (viii):

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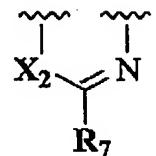
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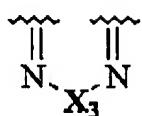
(iv)



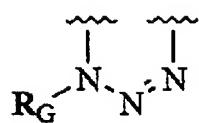
(v)



(vi)



(vii)



(viii)

one of R₅ and R₆ is H or methyl and the other of R₅ and R₆ is H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, phenyl, benzyl, or -M-E-G;

M is O, CO, SO₂, NR_J, (CO)NR_H, NR_H(CO), NR_H(SO₂), (SO₂)NR_H, or CH₂;

E is (CH₂)₁₋₄ or (CH₂)_mO(CH₂)_p where 1 ≤ (each of m and p) ≤ 3 and 2 ≤ (m + p) ≤ 4; or E is absent;

G is R_K, OR_I or NR_JR_K, provided that if p = 1, then G is H;

R₇ is H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl,

SO₂NR_H(CH₂)₂₋₄NR_JR_K, (CO)(CH₂)₂₋₄NR_JR_K or (CO)NR_H(CH₂)₂₋₄NR_JR_K;

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X_1 is O, S, NR₈, or CHR₉; X_2 is O, S, or CHR₉; and X_3 is O or S; where if X_1 or X_2 is CHR₉, said compound may also be a tautomerized indole;

R₈ is H, C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ cycloalkyl, or (C₂₋₄ alkyl)NR_LR_M; provided R₇ and R₈ together have no more than 14 carbon atoms, exclusive of R_L, R_M, R_J and R_K;

R_G is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R₉ is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl,

C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar', where Ar' is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R_P is H, C₁₋₆ alkyl, phenyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, or (CH₂)₂₋₄NR_LR_M;

R₁₀ is H, methyl, halo, or NO₂;

R₁₁ is H, methyl, halo, or NO₂;

each of R_C, R_D, R_E, R_F, R_I, R_J, R_K, R_L and R_M is independently selected from H,

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C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; each of NR_CR_D, NR_ER_F, NR_JR_K, and NR_LR_M can also independently be morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl; and

each of R_H, R_N, and R_O is independently H, methyl, or ethyl;

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

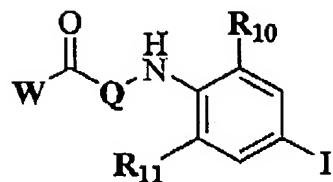
4 (previously presented). The method of claim 3, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma, vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, and arthritis pain, inclusively.

5 and 6 (canceled).

7 (previously presented). A method for treating chronic pain, wherein said chronic pain is associated with inflammation, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of the following formula (I):

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(I)

wherein

W is OR₁, NR₂OR₁, NR_AR_B, NR₂NR_AR_B, O(CH₂)₂₋₄NR_AR_B, or NR₂(CH₂)₂₋₄NR_AR_B;

R₁ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)-C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)-C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or (CH₂)₂₋₄ NR_CR_D;

R₂ is H, C₁₋₄ alkyl, phenyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical, or (C₃₋₆ cycloalkyl) methyl;

R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl, or (CH₂)₂₋₄ NR_CR_D;

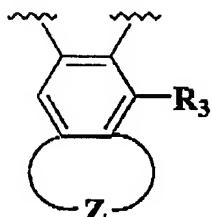
R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or phenyl;

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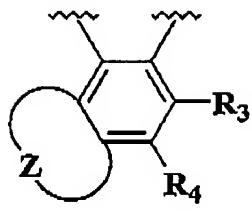
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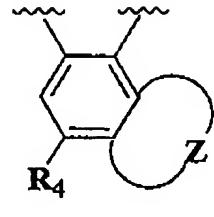
Q is one of the following formulae (i) – (iii):



(i)



(ii)



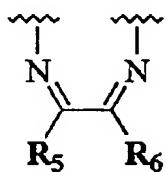
(iii)

R3 is H or F;

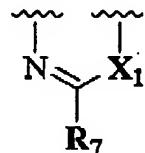
R4 is halo, NO2, SO2NR0(CH2)2-4NRERF, SO2NRERF, or (CO)T;

T is C1-8 alkyl, C3-8 cycloalkyl, (NRERF)C1-4 alkyl, ORF, -NR0(CH2)2-4NRERF, or NRERF;

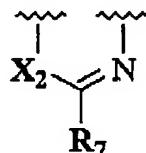
Z is one of the following formulae (iv) – (viii):



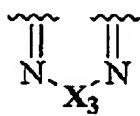
(iv)



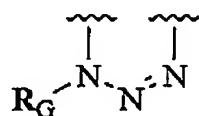
(v)



(vi)



(vii)



(viii)

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one of R_5 and R_6 is H or methyl and the other of R_5 and R_6 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, benzyl, or $\sim M-E-G$;

M is O, CO, SO_2 , NR_J , $(CO)NR_H$, $NR_H(CO)$, $NR_H(SO_2)$, $(SO_2)NR_H$, or CH_2 ;

E is $(CH_2)_{1-4}$ or $(CH_2)_m O(CH_2)_p$ where $1 \leq (each of m and p) \leq 3$ and $2 \leq (m + p) \leq 4$; or E is absent;

G is R_K , OR_I or NR_JR_K , provided that if $p = 1$, then G is H;

R_7 is H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, $(CH_2)_{1-2}Ar$, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl,

$SO_2NR_H(CH_2)_{2-4}NR_JR_K$, $(CO)(CH_2)_{2-4}NR_JR_K$ or $(CO)NR_H(CH_2)_{2-4}NR_JR_K$;

X_1 is O, S, NR_8 , or CHR_9 ; X_2 is O, S, or CHR_9 ; and X_3 is O or S; where if X_1 or X_2 is CHR_9 , said compound may also be a tautomerized indole;

R_8 is H, C_{1-4} alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, $(CH_2)_{1-2}Ar$, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, or $(C_{2-4} \text{ alkyl})NR_LR_M$; provided R_7 and R_8 together have no more than 14 carbon atoms, exclusive of R_L , R_M , R_J and R_K ;

R_G is C_{1-4} alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_{3-4} alkenyl, C_{3-4} alkynyl, C_{3-6} cycloalkyl, $(CO)OR_P$, $(C_{2-4} \text{ alkyl})NR_LR_M$, $(CO)NR_N(CH_2)_{2-4}NR_LR_M$, $(CO)(CH_2)_{2-4}NR_LR_M$, or $(CH_2)_{1-2}Ar$, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R_9 is C_{1-4} alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_{2-4} alkenyl, C_{2-4} alkynyl,

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C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar', where Ar' is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R_P is H, C₁₋₆ alkyl, phenyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, or (CH₂)₂₋₄ NR_LR_M;

R₁₀ is H, methyl, halo, or NO₂;

R₁₁ is H, methyl, halo, or NO₂;

each of R_C, R_D, R_E, R_F, R_I, R_J, R_K, R_L and R_M is independently selected from H, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; each of NR_CR_D, NR_ER_F, NR_JR_K, and NR_LR_M can also independently be morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl; and

each of R_H, R_N, and R_O is independently H, methyl, or ethyl;

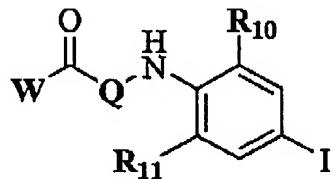
wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂; or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

8 (previously presented). A method for treating chronic pain, wherein said chronic pain is associated with arthritis, said method comprising administering to

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a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of the following formula (I):



(I)

wherein

W is OR₁, NR₂OR₁, NR_AR_B, NR₂NR_AR_B, O(CH₂)₂₋₄NR_AR_B, or NR₂(CH₂)₂₋₄NR_AR_B;

R₁ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)-C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)-C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or (CH₂)₂₋₄ NR_CR_D;

R₂ is H, C₁₋₄ alkyl, phenyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical, or (C₃₋₆ cycloalkyl) methyl;

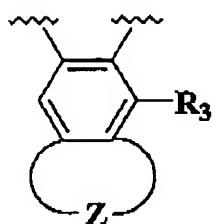
R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl, or (CH₂)₂₋₄ NR_CR_D;

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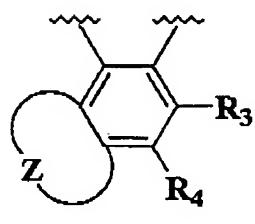
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R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or phenyl;

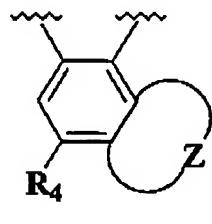
Q is one of the following formulae (i) – (iii):



(i)



(ii)



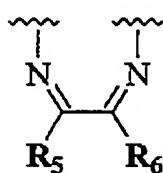
(iii)

R_3 is H or F;

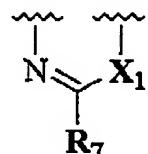
R_4 is halo, NO₂, SO₂NR₀(CH₂)₂₋₄NR_ER_F, SO₂NR_ER_F, or (CO)T;

T is C₁₋₈ alkyl, C₃₋₈ cycloalkyl, (NR_ER_F)C₁₋₄ alkyl, OR_F, -NR₀(CH₂)₂₋₄NR_ER_F, or NR_ER_F;

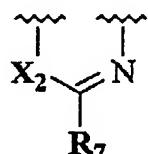
Z is one of the following formulae (iv) – (viii):



(iv)



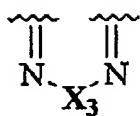
(v)



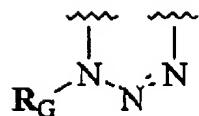
(vi)

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(vii)



(viii)

one of R_5 and R_6 is H or methyl and the other of R_5 and R_6 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-4} alkynyl, phenyl, benzyl, or $-\text{M}-\text{E}-\text{G}$;

M is O, CO, SO_2 , NR_1 , $(\text{CO})\text{NR}_1$, $\text{NR}_1(\text{CO})$, $\text{NR}_1(\text{SO}_2)$, $(\text{SO}_2)\text{NR}_1$, or CH_2 ;

E is $(\text{CH}_2)_{1-4}$ or $(\text{CH}_2)_m \text{O}(\text{CH}_2)_p$ where $1 \leq$ (each of m and p) ≤ 3 and $2 \leq (m + p) \leq 4$; or E is absent;

G is R_K , OR_1 or NR_1R_K , provided that if $p = 1$, then G is H;

R_7 is H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, $(\text{CH}_2)_{1-2}\text{Ar}$, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl,

$\text{SO}_2\text{NR}_1(\text{CH}_2)_{2-4}\text{NR}_1\text{R}_K$, $(\text{CO})(\text{CH}_2)_{2-4}\text{NR}_1\text{R}_K$ or $(\text{CO})\text{NR}_1(\text{CH}_2)_{2-4}\text{NR}_1\text{R}_K$;

X_1 is O, S, NR_8 , or CHR_9 ; X_2 is O, S, or CHR_9 ; and X_3 is O or S; where if X_1 or X_2 is CHR_9 , said compound may also be a tautomerized indole;

R_8 is H, C_{1-4} alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, $(\text{CH}_2)_{1-2}\text{Ar}$, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6}

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cycloalkyl, or (C₂₋₄ alkyl)NR_LR_M; provided R₇ and R₈ together have no more than 14 carbon atoms, exclusive of R_L, R_M, R_J and R_K;

R_G is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂, 4NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R₉ is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl,

C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar', where Ar' is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R_P is H, C₁₋₆ alkyl, phenyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, or (CH₂)₂₋₄ NR_LR_M;

R₁₀ is H, methyl, halo, or NO₂;

R₁₁ is H, methyl, halo, or NO₂;

each of R_C, R_D, R_E, R_F, R_I, R_J, R_K, R_L and R_M is independently selected from H, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; each of NR_CR_D, NR_ER_F, NR_JR_K, and NR_LR_M can also independently be morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl; and

each of R_H, R_N, and R_O is independently H, methyl, or ethyl;

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo,

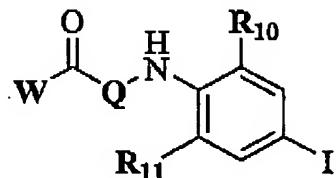
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C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

9 (previously presented). A method for treating chronic pain, wherein said chronic pain is associated with post-operative pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of the following formula (I):



(I)

wherein

W is OR₁, NR₂OR₁, NR_AR_B, NR₂NR_AR_B, O(CH₂)₂₋₄NR_AR_B, or NR₂(CH₂)₂₋₄NR_AR_B;

R₁ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (phenyl)-C₁₋₄ alkyl, (phenyl)C₃₋₄ alkenyl, (phenyl)C₃₋₄ alkynyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (C₃₋₈ heterocyclic radical)-C₃₋₄ alkenyl, (C₃₋₈ heterocyclic radical)C₃₋₄ alkynyl or (CH₂)₂₋₄NR_CR_D;

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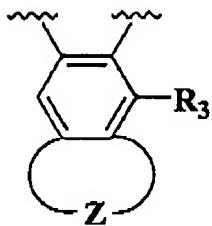
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R_2 is H, C₁₋₄ alkyl, phenyl, C₃₋₆ cycloalkyl, C₃₋₆ heterocyclic radical, or (C₃₋₆ cycloalkyl) methyl;

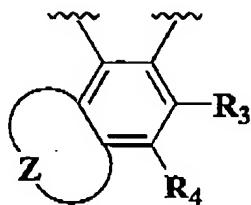
R_A is H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, phenyl, (C₃₋₈ cycloalkyl)C₁₋₄ alkyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkenyl, (C₃₋₈ cycloalkyl)C₃₋₄ alkynyl, C₃₋₈ heterocyclic radical, (C₃₋₈ heterocyclic radical)C₁₋₄ alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C₁₋₄ alkyl, (aminosulfonyl)C₁₋₆ alkyl, (aminosulfonyl)C₃₋₆ cycloalkyl, [(aminosulfonyl)C₃₋₆ cycloalkyl]C₁₋₄ alkyl, or (CH₂)₂₋₄ NR_CR_D;

R_B is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, C₃₋₈ cycloalkyl, or phenyl;

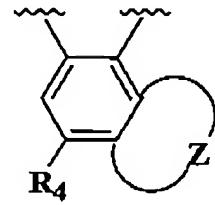
Q is one of the following formulae (i) – (iii):



(i)



(ii)



(iii)

R_3 is H or F;

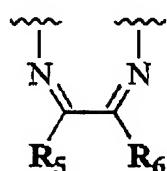
R_4 is halo, NO₂, SO₂NR_O(CH₂)₂₋₄NR_ER_F, SO₂NR_ER_F, or (CO)T;

T is C₁₋₈ alkyl, C₃₋₈ cycloalkyl, (NR_ER_F)C₁₋₄ alkyl, OR_F, -NR_O(CH₂)₂₋₄NR_ER_F, or NR_ER_F;

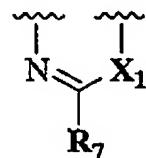
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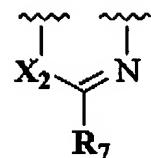
Z is one of the following formulae (iv) – (viii):



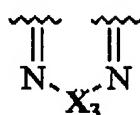
(iv)



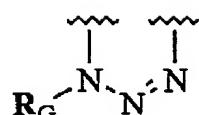
(v)



(vi)



(vii)



(viii)

one of R₅ and R₆ is H or methyl and the other of R₅ and R₆ is H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, phenyl, benzyl, or -M-E-G;

M is O, CO, SO₂, NR_J, (CO)NR_H, NR_H(CO), NR_H(SO₂), (SO₂)NR_H, or CH₂;

E is (CH₂)₁₋₄ or (CH₂)_mO(CH₂)_p where 1 ≤ (each of m and p) ≤ 3 and 2 ≤ (m + p) ≤ 4; or E is absent;

G is R_K, OR_I or NR_JR_K, provided that if p = 1, then G is H;

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R₇ is H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ cycloalkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl,

SO₂NR_H(CH₂)₂₋₄NR_JR_K, (CO)(CH₂)₂₋₄NR_JR_K or (CO)NR_H(CH₂)₂₋₄NR_JR_K;

X₁ is O, S, NR₈, or CHR₉; X₂ is O, S, or CHR₉; and X₃ is O or S; where if X₁ or X₂ is CHR₉, said compound may also be a tautomerized indole;

R₈ is H, C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ cycloalkyl, or (C₂₋₄ alkyl)NR_LR_M; provided R₇ and R₈ together have no more than 14 carbon atoms, exclusive of R_L, R_M, R_J and R_K;

R_G is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R₉ is C₁₋₄ alkyl, phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl,

C₃₋₆ cycloalkyl, (CO)OR_P, (C₂₋₄ alkyl)NR_LR_M, (CO)NR_N(CH₂)₂₋₄NR_LR_M, (CO)NR_LR_M, (CO)(CH₂)₂₋₄-NR_LR_M, or (CH₂)₁₋₂Ar', where Ar' is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R_P is H, C₁₋₆ alkyl, phenyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, or (CH₂)₂₋₄NR_LR_M;

R₁₀ is H, methyl, halo, or NO₂;

R₁₁ is H, methyl, halo, or NO₂;

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each of R_C , R_D , R_E , R_F , R_I , R_J , R_K , R_L and R_M is independently selected from H, C₁₋₄ alkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, C₃₋₆ cycloalkyl, and phenyl; each of $NR_C R_D$, $NR_E R_F$, $NR_J R_K$, and $NR_L R_M$ can also independently be morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl; and

each of R_H , R_N , and R_O is independently H, methyl, or ethyl;

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₇ ester thereof.

10 (previously presented). A method of claim 8, wherein Q is formula (i).

11 (original). A method of claim 10, wherein R₃ is H or fluoro.

12 (original). A method of claim 11, wherein R₄ is fluoro, chloro, or bromo.

13 (previously presented). A method of claim 8, wherein R₁₀ is hydrogen, methyl, fluoro, or chloro.

14 (previously presented). A method of claim 8, wherein R₁₁ is methyl, chloro, fluoro, nitro, or hydrogen.

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15 (original). A method of claim 14, wherein R₁₁ is H.

16 (original). A method of claim 14, wherein R₁₁ is fluoro.

17 (original). A method of claim 13, wherein each of R₁₀ and R₁₁ is fluoro.

18 (previously presented). A method of claim 8, wherein R₁ is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenethyl, allyl, C₃₋₅ alkenyl, C₃₋₆ cycloalkyl, (C₃₋₅ cycloalkyl)C₁₋₂ alkyl, (C₃₋₅ heterocyclic radical)C₁₋₂ alkyl, or (CH₂)₂₋₄ NR_CR_D.

19 (original). A method of claim 18, wherein R₁ is H or (C₃₋₄ cycloalkyl)C₁₋₂ alkyl.

20 (previously presented). A method of claim 8, wherein R₂ is H or methyl.

21 (previously presented). A method of claim 8, wherein R_A has at least one hydroxyl substituent.

22 (previously presented). A compound of claim 8, wherein R_A is H, methyl, ethyl, isobutyl, hydroxyethyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylamino-ethyl; and R_B is H; or where R_B is methyl and R_A is phenyl.

23 (previously presented). A method of claim 8, wherein W is NR_AR_B or NR₂NR_AR_B.

24 (previously presented). A method of claim 8, wherein W is NR₂(CH₂)₂₋₄ NR_AR_B or O(CH₂)₂₋₃ NR_AR_B.

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25 (previously presented). A method of claim 8, wherein W is NR₂OR₁.

26 (previously presented). A method of claim 8, wherein W is OR₁.

27 (previously presented). A method of claim 8, wherein Z is formula (v).

28 (original). A method of claim 27, wherein X₁ is NR₈, and R₇ is H.

29 (previously presented). A method of claim 8, wherein said MEK inhibitor has a structure selected from: 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1H-benzoimidazole-5-carboxylic acid.

30 (previously presented). A method of claim 8, wherein said MEK inhibitor has a structure selected from: 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1H-benzoimidazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-benzooxazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-benzothiazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-benzo[1,2,5]thiadiazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-benzo[1,2,5]oxadiazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-2-(2-hydroxyethyl)-1H-benzoimidazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-2-(2-dimethylamino-ethyl)-1H-benzoimidazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1-acetyl-benzoimidazole-5-carboxylic acid; 8-fluoro-7-(4-iodo-2-methyl-phenylamino)-quinoxaline-6-carboxylic acid; and 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1H-benzotriazole-5-carboxylic acid; and the corresponding hydroxamic acids and cyclopropylmethyl hydroxamates.

31 (previously presented). The method of claim 8 wherein said MEK inhibitor has a structure selected from: 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1H-benzoimidazole-5-carboxylic acid cyclopropylmethoxy-amide; 7-fluoro-6-(4-

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iodo-2-methyl-phenylamino)-6,7-dihydro-1*H*-benzoimidazole-5-carboxylic acid (hydrochloride); 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1*H*-benzoimidazole-5-carboxylic acid; 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-3*H*-benzoimidazole-5-carboxylic acid (2-hydroxy-ethoxy)-amide; 6-(2-chloro-4-iodo-phenylamino)-7-fluoro-1*H*-benzoimidazole-5-carboxylic acid; and 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1*H*-benzoimidazole-5-carboxylic acid pentafluorophenyl ester.

32 (previously presented). The method of claim 8 wherein said MEK inhibitor has a structure selected from: 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-1*H*-benzoimidazole-5-carboxylic acid cyclopropylmethoxy-amide; and 7-fluoro-6-(4-iodo-2-methyl-phenylamino)-3*H*-benzoimidazole-5-carboxylic acid (2-hydroxy-ethoxy)-amide.